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Clinical Study Synopsis for Public Disclosure

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The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country..

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's Policy on Transparency and Publication of Clinical Study Data**.

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Other Clinical Report

Document Number: c11684300-01

BI Trail No.:	1219.4
EudraCT No.:	2007-003742-15
BI Investigational Product:	BIBW 2948 BS inhalation powder, hard capsule for HandiHaler®
Title:	A phase II, randomised, double-blind, placebo-controlled and parallel group study to evaluate the safety and efficacy of four weeks treatment of 7.5 mg b.i.d, 15 mg q.d and 15 mg b.i.d. BIBW 2948 BS (inhalation powder, hard capsule for HandiHaler®) in patients with COPD associated with chronic bronchitis.
Clinical Phase:	II a
GCP Compliance:	Yes
Authors:	Prof. Dr. [redacted]
Principal/Coord. Investigator:	[redacted] M.D.
Institute/ Department:	[redacted]
Date of Report:	29 Jul 2016
Dates of Trial:	From 15 Sep 2008 From 16 Sep 2008
Additional Reports:	

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3. INTRODUCTION

Study results 1219.5 revealed compromising safety findings after unblinding the data for the active (BIBW2948 BS 30 mg b.i.d. and 15 mg b.i.d) vs. placebo groups. These findings comprise a significant decline in FEV1 after 4 weeks of treatment with BIBW 2948 BS at doses of 30 mg b.i.d. as well as 15 mg b.i.d., an increase in patient reported rescue medication use and cough, and an inbalance in treatment drop-outs for respiratory reasons.

In consequence it was decided to not expose further patients to doses of 15 mg b.i.d. BIBW 2948 BS or higher. Based on these results the just initiated study 1219.4 was halted.

Trial Data
FPI: 15 September 2008
LPO: 16 September 2008

Number of patient: 1 patient only enrolled and withdrew before randomisation.

PRIMARY ENDPOINT

The primary endpoint of this study will be change in CASA-Q symptom domain scores from baseline to the end of the 4-week treatment period.

SECONDARY ENDPOINTS

1 Efficacy endpoints

Secondary efficacy endpoints are the change from baseline in:

1. CASA-Q symptom domain scores
2. CASA-Q cough impact score
3. CASA-Q sputum impact score
4. 24-hour sputum wet weight
5. 24-hour sputum dry weight
6. 24-hour sputum volume
7. Cough frequency as recorded by the LifeShirt® device
8. Cough and Sputum Rating Scales
9. Patient and Physician reported impression of change (PGI-C and CGI-C)
10. Interleukin-8 (IL-8) plasma levels

2 Safety endpoints

1. Changes from baseline in lung function as measured by post-bronchodilator FEV_1
2. Changes from baseline in lung function as measured by post-bronchodilator FVC
3. Safety clinical laboratory parameters

Haematology: haemoglobin, hematocrit, erythrocytes, platelets, total leukocyte count with differential (neutrophils, lymphocytes, monocytes, eosinophils, and basophils), and absolute eosinophil count.

Biochemistry: albumin, alkaline phosphatase, calcium, chloride, creatinine, glucose, inorganic phosphorus, lactate dehydrogenase (LDH), potassium, gamma glutamyl transferase (GGT), carbohydrate deficient transferrin (CDT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), sodium, reflexive bilirubin (direct and indirect), total protein, uric acid and urea nitrogen.

4. Mean weekly morning peak expiratory flow (a.m. pre-dose measurement) as collected in the Patient Daily Diary.

5. Vital signs (PR, BP).

6. Reported adverse events.

3 Pharmacokinetics endpoints

The following pharmacokinetic endpoints will be derived from drug plasma concentrations of the main metabolite BIBW 3056 ZW to evaluate exposure to BIBW 2948 BS/ BIBW 3056 ZW.

3.1 Routine Pharmacokinetic Analyses for all patients

- $C_{max,ss}$ (maximum measured concentration of the analyte in plasma at steady state over a uniform dosing interval τ).
- $t_{max,ss}$ (time from last dosing to maximum concentration of the analyte in plasma at steady state).
- $C_{pre,ss}$ (predose steady state concentration of the analyte immediately before administration of the next dose).

3.2 Subgroup Pharmacokinetic Analyses for Selected Sites Only

17 patients per treatment group with more frequent blood sampling will take part in 6-hour post-dose measurement of the main metabolite BIBW 3056 ZW to evaluate exposure to BIBW 2948 BS/ BIBW 3056 ZW:

$AUC_{0-6,ss}$(area under the concentration-time curve of the analyze in plasma at steady state from 0 to 6 hours)

4. METHODOLOGY

N/A

5. RESULTS

N/A

6. DISCUSSION

1 subject was enrolled. The trial was terminated prior to randomization of subjects.

7. LITERATRURE REFERENCES

7.1 PUBLISHED REFERENCES

None

7.2 UNPUBLISHED REFERENCES

None